

REMARKS

Claims 1-34 and 40-44 are withdrawn from consideration. By the present amendment, Applicants canceled claim 38 and amended claims 35, 39 and 46. Claims 35-37, 39, 46, and 47 are under consideration.

Rejections under 35 U.S.C § 103(a)

Applicants wish to thank the Examiner for the withdrawal of the rejection of claims 35, 37 and 38 under 35 U.S.C. § 112, second paragraph, and for the withdrawal of the rejection of claims 35-39, 46 and 47 under 35 U.S.C. § 103(a) over Ramshaw and Haglund in view of Haglund_b and Gherardi.

On page 3 of the office action, the examiner rejects claims 35-39, 46, and 47 under 35 U.S.C. § 103(a) as allegedly being obvious over the combination of Ramshaw and Haglund in view of Haglund_b, Gherardi and newly-cited Barber et al. US20030044386 ("Barber"). As discussed below, Applicants respectfully submit that Barber adds nothing to the previously-cited references.

According to the Examiner, Ramshaw's DNA-prime/poxvirus boost technology "is clearly reproducible," and that "the principle of prime boosting was very well established with various virus vectors used for boosting." Ramshaw allegedly teaches DNA plasmid vector prime followed by boost with attenuated poxvirus vectors. The Examiner concedes that Ramshaw fails to teach using a VSV vector as a boosting composition.

In an attempt to remedy the deficiencies of Ramshaw, the Examiner alleges that Haglund "established efficacy of VSVs for both priming and boosting". Thus, the Examiner concludes, "one of skill in the art would be clearly attracted to try VSV as a preferred vector along with a plasmid vector as a prime and thus making the instant invention obvious." In addition, the Examiner cites the Barber reference for allegedly teaching recombinant VSV vectors comprising nucleic acids encoding cytokines.

Applicants respectfully disagree. Obviousness under § 103 is not established merely when one of skill in the art would be "clearly attracted to try" an element of the claimed invention from a large menu of potential gene delivery vectors. A reasonable expectation of success is required.

The Ramshaw reference states that either reversing the order of immunization or changing the nature of the boosting virus in a prime-boost immunization scheme "resulted in a failure of protection." See page 164, right column. Ramshaw thus recognized the unpredictable nature of the selection of the boosting virus, even when merely switching from one vaccinia virus to another vaccinia virus.

The results from Haglund_b further show that the order of using VSV vectors as either a priming vector or boosting vector made a difference in immune response. For example, when boosts are performed with VSV vectors following a VSV prime, the CTL responses were less focused on Gag since the internal VSV proteins are shared between the priming and boosting vectors, according to Haglund_b, p. 7515. However, when boosting with a “completely heterologous VV-Gag vector [following a VSV prime], all of the secondary responses are focused on Gag alone.” These same results from Haglund_b would discourage use of VSV as a boosting vector, and instead would suggest using VSV vectors as a priming vector.

Moreover, at the time of filing, there was a large number of vectors to choose from (see, for example, the list provided in previous response filed August 4, 2010), a large number of possible combinations of vectors, but a lack of finite number of identified, predictable vectors. For example, in a publication published two years after Ramshaw, a DNA prime-MVA boost vaccine regiment encoding HIV tat was unpredictable and unsuccessful. See abstract of Allen et al. *J Virol.* 2002 April; 76(8): 4108–4112 (of record), which states: “Despite the induction of Tat-specific CTL, there was no significant reduction in either peak or viral set point compared to that of controls.”

The Barber reference also fails to rectify the deficiencies of the remaining cited references to arrive at the claimed invention. The Barber reference teaches use of VSV as a vector to deliver a cytokine as a therapeutic itself for cancer therapy- not as a vaccine adjuvant as it is intended in the claimed invention. See, for example, Barber abstract.

As amended, the claimed invention requires a second DNA plasmid that encodes a cytokine and that is co-administered with a first DNA plasmid encoding the antigen. This is nowhere taught or suggested by Barber. Support for the amendment of claim 35 is found in canceled claim 38, as well as the following portions of the published patent application: Paragraph 9, last two lines; paragraph 37, first six lines; and paragraph 39, first eight lines

Accordingly, none of the references individually or in combination teach or disclose a composition that includes a DNA plasmid encoding an antigen and a DNA plasmid encoding a cytokine in combination with a VSV encoding the antigen, nor was there any teaching of a reasonable expectation of success for immunogenicity of such composition. The Examiner is respectfully directed to pages 20-23 of Applicants’ August 4, 2010 submission for a discussion of the case law, including the Supreme Court’s *KSR* decision, which supports the unobviousness of Applicants’ claims.

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In view of the foregoing discussion, applicants submit that the present application is in condition for allowance. Reconsideration and allowance are respectfully requested.

If a telephone conference would advance prosecution of this application, the Examiner is invited to telephone the undersigned at 845-602-3144.

Respectfully submitted,

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